

WE CLAIM:

1. A compound comprising a plurality of linked nucleosides, wherein at least one of said nucleosides is functionalized at its 2'-position by attachment of a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent.

2. The compound of claim 1 wherein a linking moiety attaches said steroid molecule, reporter molecule, non-aromatic lipophilic molecule, reporter enzyme, peptide or protein to the 2'-position of said functionalized nucleoside.

3. The compound of claim 1 wherein said functionalized nucleoside comprises a steroid molecule, biotin, a fluorescein dye molecule, an alicyclic hydrocarbon molecule, a saturated or unsaturated fatty acid, a wax, a terpene, a polycyclic hydrocarbon, adamantane, a buckminsterfullerene, a reporter enzyme, a peptide, a protein, thiamine, riboflavin, nicotinic acid, niacin, pyridoxal, pantothenic acid, biotin, folic acid, methyl folate, a vitamin B₁₂ cobamide coenzyme, inositol, choline, ascorbic acid, retinoic acid, retinol, a tocopherol, vitamin D, vitamin K, EDTA, DTPA, o-phenanthroline, a photonuclease/intercalator, an aryl azide photo-crosslinker, a phenanthroline/metal complex and a bipyridine/metal complex attached to the 2'-position of said nucleoside.

4. The compound of claim 1 wherein said functionalized nucleoside comprises a steroid molecule attached via a linking moiety to the 2'-position of said nucleoside.

5. The compound of claim 2 wherein said linking moiety comprises an Ω -aminoalkoxy or Ω -aminoalkylamino moiety.

6. The compound of claim 5 wherein said linking moiety comprises an Ω -aminoalkoxy moiety.

7. The compound of claim 1 wherein said functionalized nucleoside comprises a reporter enzyme, a peptide or protein attached via a linking moiety to the 2'-position of said nucleoside.

8. The compound of claim 1 wherein cholic acid, deoxycholic acid, dehydrocholic acid, cortisone, digoxigenin, testosterone, cholesterol or digoxigenin is attached at the 2' position of said nucleoside.

9. The compound of claim 8 wherein attachment is through a linking moiety comprises an Ω -aminoalkoxy or Ω -aminoalkylamino moiety.

10. The compound of claim 9 wherein said linking moiety comprises an Ω -aminoalkoxy moiety.

11. The compound of claim 10 wherein said linking moiety comprises a 5-aminopentoxy group.

12. The compound of claim 1 wherein cholic acid is attached at the 2' position of said nucleoside.

13. The compound of claim 12 wherein said attachment is through a linking moiety comprises an Ω -aminoalkoxy or Ω -aminoalkylamino moiety.

14. The compound of claim 13 wherein said linking moiety comprises an Ω -aminoalkoxy moiety.

15. The compound of claim 14 wherein said linking moiety comprises a 5-aminopentoxy group.

16. The compound of claim 1 wherein at least one of the linked nucleosides is a 2'-deoxy-2'-fluoro, 2'-methoxy, 2'-ethoxy, 2'-propoxy, 2'-aminoalkoxy or 2'-allyloxy nucleoside.

17. The compound of claim 1 wherein at least two of the linked nucleosides are linked by phosphorothioate linking groups.

18. A compound comprising a plurality of linked nucleosides, wherein at least one of the nucleosides is a functionalized nucleoside selected from the group consisting of:

a 2' functionalized nucleoside having cholic acid linked to the 2' position of the nucleoside;

a heterocyclic base functionalized nucleoside having cholic acid linked to the heterocyclic base of the nucleoside;

a 5' terminal nucleoside having cholic acid linked to the 5'-position of the nucleoside;

a 3' terminal nucleoside having cholic acid linked to the 3'-position of the nucleoside; and

an inter-strand nucleoside having cholic acid linked to an inter-nucleotide linkage linking said inter-strand nucleoside to an adjacent nucleoside.

19. The compound of claim 18 wherein a linking group links said cholic acid and the functionalized nucleoside.

20. The compound of claim 18 wherein said functionalized nucleoside is a 2' functionalized nucleoside having cholic acid linked to the 2'-position of the nucleoside.

21. The compound of claim 18 wherein at least one of the linked nucleosides is a 2'-deoxy'-2'-fluoro, 2'-methoxy, 2'-ethoxy, 2'-propoxy, 2'-aminoalkoxy or 2'-allyloxy nucleoside.

22. The compound of claim 18 wherein at least two of the linked nucleosides are linked by phosphorothioate linking groups.

23. The compound of claim 18 wherein said functionalized nucleoside is a 3' terminal nucleoside having cholic acid linked to the 3'-position of said 3' terminal nucleoside.

24. The compound of claim 18 wherein said functionalized nucleoside is a 5' terminal nucleoside having cholic acid linked to the 5'-position of said 5' terminal nucleoside.

25. The compound of claim 18 wherein said functionalized nucleoside is a heterocyclic base functionalized nucleoside having cholic acid linked to the heterocyclic base of said nucleoside.

26. The compound of claim 18 wherein said functionalized nucleoside is an inter-strand nucleoside having cholic acid linked to an inter-nucleotide linkage linking said inter-strand nucleoside to an adjacent nucleoside.

27. A compound comprising a plurality of linked nucleosides, wherein:

at least one of the nucleosides is a 2'-deoxy'-2'-fluoro, 2'-O-C₁-C₂₀-alkyl, 2'-O-C₂-C₂₀-alkenyl, 2'-O-C₂-C₂₀-alkynyl, 2'-S-C₁-C₂₀-alkyl, 2'-S-C₂-C₂₀-alkenyl, 2'-S-C₂-C₂₀-alkynyl, 2'-NH-C₁-C₂₀-alkyl, 2'-NH-C₂-C₂₀-alkenyl, 2'-NH-C₂-C₂₀-alkynyl nucleoside; and

at least one of the nucleosides is a functionalized nucleoside selected from the group comprising::

a 2'-functionalized nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the 2'-position of the nucleoside;

a heterocyclic base functionalized nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the heterocyclic base of the nucleoside;

a 5' terminal nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the 5'-position of the nucleoside;

a 3' terminal nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the 3'-position of the nucleoside; and

an inter-strand nucleoside having a steroid molecule, a reporter molecule, a non-aromatic

lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to an inter-stand linkage linking said inter-strand nucleoside to an adjacent nucleoside.

28. The compound of claim 27 wherein:

said functionalized nucleoside is a nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the 2'-position of said nucleoside; and

the remainder of said linked nucleosides are 2'-deoxy-2'-fluoro, 2'-methoxy, 2'-ethoxy, 2'-propoxy, 2'-aminoalkoxy or 2'-allyloxy nucleosides.

29. The compound of claim 27 wherein said functionalized nucleoside is a 3' terminal nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the 3'-position of the nucleoside.

30. The compound of claim 27 wherein said functionalized nucleoside is a 5' nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a

hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the 5'-position of the nucleoside.

31. The compound of claim 27 wherein said functionalized nucleoside is a heterocyclic base functionalized nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to the heterocyclic base of the nucleoside.

32. The compound of claim 27 wherein said functionalized nucleoside is an inter-strand nucleoside having a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent linked to an inter-strand linkage linking said nucleoside to an adjacent nucleoside.

33. The compound of claim 27 wherein at least two of the linked nucleosides are linked by phosphorothioate linking groups.

34. A method of effecting cellular uptake of a compound having a plurality of linked nucleosides, comprising contacting an organism with said compound wherein said compound includes at least one nucleoside functionalized at its 2'-position by attachment of a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, and a lipid soluble vitamin to the 2'-position with a linking moiety.

35. The method of claim 34 further including selecting said steroid molecule from the group consisting of cholic acid, deoxycholic acid, dehydrocholic acid, cortisone, digoxigenin, testosterone, cholesterol and digoxigenin.

36. The method of claim 34 further including selecting cholic acid as said steroid molecule.

37. The method of claim 34 further including selecting an Ω -aminoalkylamino moiety as said linking molecule.

38. A method of enhancing an antisense oligonucleotide comprising:

functionalizing said oligonucleotide with at least one of a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent; and

further functionalizing said oligonucleotide with one of a group to effect increase affinity of said oligonucleotide for a target or a group to increase the stability of said oligonucleotide to nucleases.

39. The method of claim 38 wherein said oligonucleotide is functionalized with one of a steroid molecule, biotin, a fluorescein dye molecule, an alicyclic hydrocarbon molecule, a saturated or unsaturated fatty acid, a wax, a terpene, a polycyclic hydrocarbon, adamantine, a buckminsterfullerene, a reporter enzyme, a peptide, a protein, pyrene, thiamine, riboflavin, nicotinic acid, niacin, pyridoxal, pantothenic acid, biotin, folic acid, methyl folate, a vitamin B_{12} cobamide coenzyme, inositol, choline, ascorbic acid, retinoic acid, retinol, a tocopherol,

vitamin d, vitamin K, EDTA, DTPA, o-phenanthroline, a photonuclease/intercalator, a bipyridine complex, an aryl azide photo-crosslinker, a phenanthroline/metal complex or a bipyridine/metal complex.

40. The method of claim 38 including further functionalizing said oligonucleotide to both increase affinity of said oligonucleotide for a target and to increase the stability of said oligonucleotide to nucleases.

41. A compound comprising a plurality of linked nucleosides, wherein at least one of the nucleosides is a functionalized nucleoside selected from the group consisting of:

a 2' functionalized nucleoside having folic acid linked to the 2' position of the nucleoside;

a heterocyclic base functionalized nucleoside having folic acid linked to the heterocyclic base of the nucleoside;

a 5' terminal nucleoside having folic acid linked to the 5'-position of the nucleoside;

a 3' terminal nucleoside having folic acid linked to the 3'-position of the nucleoside; and

an inter-strand nucleoside having folic acid linked to an inter-nucleotide linkage linking said inter-strand nucleoside to an adjacent nucleoside.

42. A compound of claim 41 wherein said functionalized nucleoside is a 2' functionalized nucleoside having folic acid linked to the 2' position of the nucleoside.

43. A compound comprising a plurality of linked nucleosides, wherein at least one of the nucleosides is a functionalized nucleoside selected from the group consisting of:

a 2' functionalized nucleoside having pyrene linked to the 2' position of the nucleoside;

a 5' terminal nucleoside having pyrene linked to the 5'-position of the nucleoside;

a 3' terminal nucleoside having pyrene linked to the 3'-position of the nucleoside; and

an inter-strand nucleoside having pyrene linked to an inter-nucleotide linkage linking said inter-strand nucleoside to an adjacent nucleoside.

44. A compound of claim 43 wherein said functionalized nucleoside is a 2' functionalized nucleoside having pyrene linked to the 2' position of the nucleoside.